REMARKS

Introduction

Claims 1, 7, 10, 11, 14-16, 19, 25, 30, 39, 43-46, 54, 56-62, 66, 89, 90, 93, and 96 are currently pending. Applicants have amended claim 1, which enjoys support at page, for example at paragraph [094] of the application as published, US Patent Application Publication No. 20080060093, and cancelled claims 2 and 3. No new matter has been introduced by way of these amendments. Applicants have amended the claims without prejudice to their future prosecution in this or other continuing application.

Applicants thank the Examiner for withdrawing rejections under 35 USC 101.

The rejection under 35 USC 112, 1st paragraph (enablement) should be withdrawn: the claims are fully enabled

Applicants respectfully request the Office to withdraw its rejection under 35 USC 112, 1st paragraph (enablement). The amended claims are fully enabled by the specification as filed.

The Office again has relied on the post-filing art of Tek (*Chromosome Research* 18:337-347, 2010; "Tek"), allegedly, to demonstrate that which was not known in the art at the time of filing, and is still not known in the art, "namely, which sequences are required for centromere formation and function." The Office asserts that Tek indicated that the claimed sequence, SEQ ID NO:24, "is not likely to be the only required sequence for such function, and therefore when determining whether one has a product of the instant invention or not, one must be able to determine by structure which embodiment are functional and which are not..." (page 6 of the action).

Applicants note: (1) by definition, an invention is something that was not known previously in the art, "namely, which sequences are required for centromere formation and function:" while SEQ ID NO:24 had previously been identified as a centromeric repeat, not

until Applicants' invention had the claim-recited repeat (SEQ ID NO: 24) been shown to confer function. Tek used ChIP analysis, not any kind of cell division analysis, to identify CENH3-associated sequences – ChIP implies function, but does not prove it – as the Office admitted in its previous action, and (2) Applicants have fully enabled the present claims.

It is illogical for the Office to assert that Tek demonstrates that which is unpredictable in the art when Tek did *not* do the same, or even similar, experiments as Applicants to enable the presently pending claims, e.g. experiments described in Example 10. Similarly, it is illogical to rely on Tek to demonstrate that which is not known in the art when Tek did *not* test their identified sequences for function, but relied only on association to CENH3, and when, in fact, Applicants have tested their identified sequence for function. Furthermore, Applicants *have* demonstrated that SEQ ID NO:24 confers centromere function. Thus, the application of the post filing art of Tek to the instant invention is inappropriate.

The Office also rejected Applicants' arguments because "the above mini-chromosomes [SB6 and SB12] comprise additional sequences which the claims as currently written, are not limited to." (page 6 of the action). The Office seems to be of the opinion that additional sequences are required for centromere function, that are not presently recited for the claim to be operable.

Applicants note that *MPEP 2164.05* prescribes that the Office weigh enablement based on evidence as a whole, "The examiner must then weigh all the evidence before him or her, including the specification and any new evidence supplied by applicant with the evidence and/or sound scientific reasoning previously presented in the rejection and decide whether the claimed invention is enabled. The examiner should **never** make the determination based on personal opinion. The determination should always be based on the weight of all the evidence" *MPEP 2164.05* (emphasis not added). Applicants have demonstrated and given more than ample evidence for enablement of the pending claims, that the presently presented claims are fully enabled by Applicants' specification.

The Office should present clearly convincing evidence that other sequences are required for centromere function than what is currently claimed. Applicants have presented clear and convincing evidence, including evidence of autonomy (paragraphs [0444]-[0446] of

the application as published), which inherently meets the claim limitation of transmission efficiency of at least 90% (see the discussion below for written description).

Applicants respectfully re-present their discussion from their previous response.

The Office cited Tek as evidence that the instant application is non-enabled because Office avers that Tek shows that GmCent-1 and GmCent-2 repeats are necessary for centromere function. Applicants respectfully traverse because Tek did not show that the centromeric sequences Tek identified *are required* for centromere function.

The Office cited Tek as evidence that the location of a sequence in the centromeric region is not sufficient to confer centromere function and to demonstrate that more than one type of sequence that interacts with histones (CENH3) may be necessary for kinetochore function in soybeans. However, the studies in Tek did not test the ability of the identified sequences to segregate to daughter cells during cell division and instead relied on ChIP experiments using CENH3 combined with FISH and sequence analysis to demonstrate the localization of sequence to the centromeric region. The Office acknowledges that merely identifying sequences that react with CENH3 does not appear to be sufficient to give guidance to the sequences that confer centromeric function (Office Action of December 23, 2010; page 5, last paragraph to page 6). Thus, the teachings in Tek do not support the Office's assertion that the pending claims are not enabled by the specification. Contrary to the teaching in Tek, Applicants have not relied on CENH3 as the key to centromeric function, but instead, have used functional assays that demonstrate that the presently claimed invention is fully enabled. In working Example 10 of the specification as filed (paragraphs [0432] to [0448]; citations are to the published application, US Publication No. 20080060093), Applicants demonstrated that a mini-chromosome derived from BAC SB12 comprising SEQ ID NO:24 was retained as an autonomous, circular mini-chromosome in transgenic soybean cells that had been propagated for 5 months (paragraph [0444]). Applicants demonstrated that this mini-chromosome was autonomous by two independent criteria: (1) mini-chromosome rescue (paragraphs [0444] to [0445]), and (2) FISH analysis (paragraph [0446]). In the rescue experiments, antibiotic-resistant (a trait carried on the mini-chromosome construct and not native to the soybean genome) colonies were observed from DNA extracted from cells treated and

untreated with exonuclease (linear DNA is susceptible to exonuclease, while circular DNA is resistant), but no antibiotic resistant colonies were observed in exonuclease-treated controls (paragraph [0444]. In FISH analysis, Applicants observed staining of an autonomous, circular mini-chromosome and in the same line, no integrated copies of the construct into the native genome. Centromere staining was also observed. Applicants also sequenced two mini-chromosomes, one derived from the SB12 BAC used in the autonomy analyses, and SB6 (paragraphs [0447] to [0448]). This sequence analysis demonstrated that in the SB12-derived mini-chromosome 80% of the insert was composed of tandem satellite repeats, 9.9% made up of retroelement-related sequences, and 10.1% representing novel, contiguous sequence (paragraph [0448]). All of the results provided in Example 10 demonstrate that the invention as presently claimed, is fully enabled.

Applicants also note that the Office has mis-applied a post-filing reference in its enablement rejection, for which the *MPEP* gives clear guidance. "In general, the examiner should not use post-filing date references to demonstrate that the patent is non-enabling. Exceptions to this rule could occur if a later-dated reference provides evidence of what one skilled in the art would have known on or before the effective filing date of the patent application. *In re Hogan*, 559 F.2d 595, 605, 194 USPQ 527, 537 (CCPA 1977Tek does not show what was not known at the time of filing or that the invention, as presently claimed, does not work. Tek shows, at best, that the GmCent-4 repeats can be found in centromeric regions, but did not state that both GmCent-1 and GmCent-4 repeats are *necessary* for centromere function. In fact, Tek makes no assertion about the ability of any of the identified sequences to function together or individually as centromere sequences. Tek does *not* state that the present invention as claimed was not possible at the time the present application was filed. Tek is simply unable to do so because Tek does not describe any experiments where the identified sequences were tested for their ability to segregate to daughter cells during cell division. Applicants, however, have performed such experiments, as discussed above.

Furthermore, the Office seems to acknowledge that Tek does not make any final, functional conclusions regarding Tek's findings and centromere function by stating Tek "discloses the sequences *believed* to be necessary for centromere function in soybeans and

disclose that 3 distinct repeats *appear* to be necessary for centromere function, GmCent-1, GmCent-4, and GmCR...." Nowhere does Tek say that all the identified sequences are, or any particular sequence is, essential for soybean centromere function. Thus, the Office's reliance on the teachings in Tek to support the rejection for lack of enablement is improper. The pending claims are enabled by the specification for the reasons set out above and in the previous response, therefore the rejection under 35 USC 112, first paragraph for lack of enablement should be withdrawn.

The rejection under 35 USC 112 – written description should be withdrawn: the amended claims are fully described in the specification

The Office is respectfully requested to withdraw the rejections under 35 USC 112 – written description because (1) Applicants' amendment obviates in part the rejection in deleting the alternative of a fragment of SEQ ID NO:24; and (2) Applicants have fully described functional centromere sequences, and minichromosomes comprising the same.

Applicants argued, as described below, that Applicants have fully described the SEQ ID NO:24 as a functional centromeric repeat, but the Office found the argument non-persuasive because "...the example neither demonstrates, indicates or discusses transmission efficiency, and therefore does not meet the 90% transmission rate required by the claims" (page 10 of the Action). In order to expedite prosecution, Applicants have amended the claims by deleting the transmission rate limitation; thus the rejection is obviated by amendment.

As a courtesy, Applicants reiterate their arguments from their previous action.

Applicants fully described and produced autonomous, circular mini-chromosomes comprising SEQ ID NO:24 (thus defining the invention by its physical and chemical properties as required by, for example, *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd*, 18 USPI 2d, 1016 at 1021, (Fed Cir. 1991)) as shown in Example 10 - contrary to the Office's assertion that Applicants have not produced any such working examples.

The Office appears to be relying on the post-filing art of Tek in asserting that the specification does not described all the necessary sequence for centromere function and does not describe what is necessary for the claimed function. Tek did not test any centromeric

sequences for the ability to segregate to daughter cells during cell division. As the Office noted, "merely identifying sequences that react with CENH3, in light of the art above [referring to Tek], does not appear to be sufficient to give guidance as to sequences that confer centromeric function" (Office Action of December 23, 2010, page 5, last paragraph to page 6). Tek identified centromeric sequences by their ability to interact with CENH3, uncoupled with any functional assay that tests centromere function.

In view of the teachings in working Example 10, the specification clearly describes the necessary structural features for conferring the ability to segregate to daughter cells. Therefore, the rejection under 35 USC 112, first paragraph for lack of adequate written description should be withdrawn.

CONCLUSION

Applicants respectfully request timely allowance of the pending claims. Should the Office feel that there are any issues outstanding after consideration of the response; the Office is invited to contact the Applicant's undersigned representative to expedite prosecution.

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Dated: January 31, 2011

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